CLAIMS

What is claimed is:

1. A method for assaying molecules in a sample comprising the steps of:

- providing a sample which contains one or more target molecules or molecular complexes;

- contacting said target with one or more probes under conditions which permit the formation of a target-probe complex, wherein the probe comprises one or more magnetic labels;

- subjecting said target-probe complex to an applied magnetic field; and

- determining one or more magnetic characteristics of said target-probe complex.

2. The method of Claim 1, wherein said target molecule or molecular complex is disposed on a support.

3. The method of Claim 2, wherein said target molecule or molecular complex is disposed on the support on an array.

4. The method of Claim 3, wherein said array comprises an addressable array.

5. The method of Claim 1, wherein said probe is disposed on a support.

6. The method of Claim 5, wherein said probe is disposed on the support on an array.

7. The method of Claim 6, wherein said array is an addressable array.

8. The method of Claim 1, wherein said determining comprises measuring the magnetization of said target-probe complex in response to said applied magnetic field.

9. The method of Claim 1, wherein said determining comprises providing magnetic sensing means that generates a signal in response to said magnetic characteristic.

10. The method of Claim 9, wherein said sensing means comprises a giant magnetoresistive ratio sensor.

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11. The method of Claim 9, wherein said determining comprises providing signal processing means that generates readable output from said signal.

12. The method of Claim 1, wherein said determining comprises moving the support or the sensor in relation to the other in one or more directions by transportation means.

13. The method of Claim 1, further comprising subjecting said target-probe complex to one or more of a plurality of applied magnetic fields having different intensities.

14. The method of Claim 1, further comprising subjecting said target-probe complex to one or more of a plurality of applied magnetic fields having different directions.

15. The method of Claim 1, further comprising contacting the target molecule or molecular complex with a non-magnetic colloid.

16. The method of Claim 1, wherein said probe is joined to one or more colored beads, fluorescent beads, or fluorescent cells.

17. The method of Claim 16, further comprising the step of detecting the presence of said target-probe complex by visual, electronic or optical means.

18. A method of isolating one or more biomolecules in a sample comprising the steps of:

- providing a sample containing one or more target biomolecules or molecular complexes;
- contacting the target with one or more probes under conditions which permit the formation of a target-probe complex, wherein the probe comprises one or more magnetic labels; and
- applying a magnetic field to said target-probe complex which isolates said complex according to one or more magnetic characteristics.

19. The method of Claim 18, wherein said magnetic label comprises a ferrofluid.

20. The method of Claim 18, wherein said probe is joined to one or more colored beads, fluorescent beads, or fluorescent cells.

21. The method of Claim 20, further comprising the step of detecting the presence of said target-probe complex by visual, electronic or optical means.

22. A method of identifying the presence of magnetically labeled biomolecules in a sample comprising the steps of:

- providing a sample containing one or more biomolecules;
- contacting the target biomolecule with a magnetic label under conditions which permit the formation of a biomolecule-label complex;
- subjecting said sample to an applied magnetic field; and
- detecting a characteristic response of said sample to an applied magnetic field.

23. The method of Claim 22, wherein said characteristic response is defined at least in part by an induced magnetization of said sample.

24. The method of Claim 22, wherein said characteristic response is defined at least in part by an induced orientation change of said magnetically labeled biomolecules.

25. A method for nucleic acid hybridization comprising the steps of:

- providing one or more single stranded target nucleic acids disposed on a support;
- contacting the single stranded target nucleic acid with one or more nucleic acid probes under conditions which promote the formation of a nucleic acid hybrid, wherein the nucleic acid probe comprises a nucleotide sequence complementary to the single stranded target nucleic acid;
- contacting the nucleic acid hybrid with a ferrofluid whereby the ferrofluid binds to the single stranded target nucleic acid and the nucleic acid hybrid; and
- determining a difference in magnetic signal between the single stranded target nucleic acid and the nucleic acid hybrid.

26. The method of Claim 25, further comprising contacting the single stranded target nucleic acid with a non-magnetic colloid.

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27. A method for nucleic acid hybridization comprising the steps of:

- providing a sample that may include a first or a second target nucleic acid disposed on a support;
- contacting the sample with a first nucleic acid probe under conditions which permit the formation of a first nucleic acid hybrid, wherein the first nucleic acid probe comprises a nucleic acid sequence complementary to the first target nucleic acid and a first label having a first magnetic characteristic;
- contacting the sample with a second nucleic acid probe under conditions which permit the formation of a second nucleic acid hybrid, wherein the second nucleic acid probe comprises a nucleic acid sequence complementary to the second target nucleic acid and a second label having a second magnetic characteristic; and
- identifying the presence of the first nucleic acid hybrid by detecting the first magnetic characteristic.

28. The method of Claim 27, further comprising identifying the presence of the second nucleic acid hybrid by detecting the second magnetic characteristic.

29. The method of Claim 28, wherein the presence of the first and second nucleic acid hybrids is identified by detecting one or more magnetic characteristics produced by the combined first magnetic characteristic and the second magnetic characteristic.

30. The method of Claim 27, further comprising contacting the sample with a non-magnetic colloid.

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31. A method of nucleic acid hybridization comprising the steps of:

- providing one or more single stranded nucleic acid probes joined to a support so as to form a probe-support complex;
- providing one or more single stranded target nucleic acids wherein the single stranded target nucleic acid complements the probe nucleic acid and the single stranded target nucleic acid is joined to a magnetic label;
- contacting the probe-support complex with the single stranded target nucleic acid under conditions which permit hybridization so as to form a target-probe-support complex;
- applying a magnetic field to the target-probe-support complex; and
- identifying the presence of the target-probe-support complex by an accumulation of target-probe-support complex induced by the magnetic field.

32. The method of Claim 31, wherein said probe is joined to one or more colored beads, fluorescent beads, or fluorescent cells.

33. The method of Claim 32, further comprising the step of detecting the presence of said target-probe-support complex by visual, electronic or optical means.

34. A method of increasing binding efficiency comprising the steps of:

- providing one or more target molecules or molecular complexes;
- providing one or more probes, wherein the probe comprises one or more magnetic labels; and
- guiding the probe toward the target with an applied magnetic field.

35. The method of Claim 34, further comprising guiding unbound labeled probe away from the target with an applied electric field.

36. A method for identifying the presence of a protein comprising the steps of:

- providing a target protein disposed on a support;
- contacting the disposed protein with a probe under conditions which promote the formation of a target protein-probe complex, wherein the probe comprises a domain which binds to the target protein and a magnetic label;
- subjecting said target protein-probe complex to an applied magnetic field; and
- determining a magnetic characteristic of said target protein-probe complex.

37. The method of Claim 36, wherein said determining comprises measuring the magnetization of said target protein-probe in response to said applied magnetic field.

38. The method of Claim 36, further comprising contacting the target protein with a non-magnetic colloid.

39. The method of Claim 36, wherein the probe is an antibody or fragment thereof.

40. A method for identifying the presence of a protein comprising:

- providing a target protein disposed on a support;
- contacting the target protein with a probe under conditions which promote the formation of a target protein-probe complex, wherein the probe comprises a domain which binds to the target protein;
- contacting the target protein-probe complex with a ferrofluid whereby the ferrofluid binds to the target protein and the target protein-probe complex; and
- detecting a difference in magnetic signal between the target protein and the target protein-probe complex.

41. The method of Claim 40, further comprising contacting the target protein with a non-magnetic colloid.

42. A method for identifying the presence of a protein comprising the steps of:

- providing a sample that may include a first or a second target protein disposed on a support;
- contacting the sample with a first probe under conditions which permit the formation of a first target protein-probe complex, wherein the first probe comprises a domain which binds to the target protein and a magnetic label having a first magnetic characteristic;
- contacting the sample with a second probe under conditions which permit the formation of a second target protein-probe complex, wherein the second probe comprises a domain which binds to the first target protein and a magnetic label having a second magnetic characteristic;
- identifying the presence of the first target protein-probe complex by detecting the first magnetic characteristic.

43. The method of Claim 42, further comprising identifying the presence of the second target protein-probe complex by detecting the second magnetic characteristic.

44. A method of identifying the presence of a protein comprising the steps of:

- providing a probe joined to a support so as to form a probe-support complex;
- providing a target protein, wherein the target protein interacts with the probe and the target protein is joined to a magnetic label;
- contacting the probe-support complex with the target protein under conditions which permit an interaction so as to form a target-probe-support complex;
- applying a magnetic field to the target-probe-support complex; and
- identifying the presence of the target-probe-support complex by an accumulation of target-probe-support complex induced by the magnetic field.

45. A method of competitive binding analysis comprising the steps of: providing a target biomolecule;

- contacting the target biomolecule with a first probe molecule comprising a domain which binds to the target biomolecule and a first magnetic label having a first magnetic characteristic;
- contacting the target biomolecule with a second probe molecule comprising a domain which binds to the target biomolecule at the same site as the first probe and a second magnetic label having a second magnetic characteristic;
- identifying the presence of the first probe on the target biomolecule by detecting the first magnetic characteristic; and
- identifying the presence of the second probe on the target biomolecule by detecting the second magnetic characteristic.

46. The method of Claim 45, further comprising the step of detecting a change in the relative preponderance of the first magnetic characteristic and the second magnetic characteristic over time.

47. The method of Claim 45, further comprising contacting the target biomolecule with a non-magnetic colloid which binds to the target biomolecule.

48. A method for identifying an interaction of a probe biomolecule with a target biomolecule comprising the steps of:

- providing a target biomolecule in a fluid;
- providing a probe biomolecule which interacts with the target biomolecule, wherein said probe biomolecule comprises a magnetic label;
- contacting the target biomolecule with the probe biomolecule under conditions which permit the formation of a target biomolecule-probe complex; and
- comparing the magnetic swing of the probe biomolecule in an applied magnetic field with the magnetic swing of the target biomolecule-probe complex in an applied magnetic field.

49. A method of enhancing the binding of a probe biomolecule to a target biomolecule comprising the steps of:

- providing a target biomolecule disposed on a support;
- providing a probe biomolecule comprising a magnetic label;
- contacting the target biomolecule with the probe biomolecule, wherein the probe biomolecule interacts with the target biomolecule; and
- applying a magnetic field to the target biomolecule and the probe biomolecule such that the probe biomolecule is induced to move toward the disposed target biomolecule.

50. The method of Claim 49, wherein the magnetic field is applied in a pulsing fashion.

51. The method of Claim 50, further comprising the step of applying an electrical field and the magnetic field to the target biomolecule and the probe biomolecule such that the concentration of the probe biomolecule at a site near the disposed target biomolecule is enhanced.

52. The method of Claim 51 wherein the electric field is administered in a pulsing fashion.

53. The method of Claim 49, further comprising the step of applying an electrical field and the magnetic field to the target biomolecule and the probe biomolecule such that the concentration of the probe biomolecule at a site near the disposed target biomolecule is enhanced and by the coordination of the electrical field and the magnetic field the unbound and unlabeled probe is removed.

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54. A method of reducing non-specific binding of a probe biomolecule during a binding assay comprising the steps of:

- providing one or more target molecules or molecular complexes disposed on a support;
- contacting the target with one or more probes under conditions which permit the formation of a target-probe complex, wherein the probe comprises one or more magnetic labels;
- subjecting said target-probe complex to an applied magnetic field; and
- administering an electrical field and a magnetic field to the support and the probesuch that non-specifically bound probe is separated from the target biomolecule.

55. The method of Claim 54, further comprising administering a pulsing electrical field and a pulsing magnetic field to the support and the probe biomolecule.

56. A method of nucleic acid separation comprising the steps of:

- providing a sample having one or more polynucleotides in a solution;
- contacting the sample with a ferrofluid whereby the ferrofluid binds to one or more polynucleotides;
- administering a magnetic field to the sample such that one or more of nucleic acids are induced to separate according to their mass.

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57. An apparatus for detecting a target molecular species, comprising:

- a magnetoresistive or magnetostrictive magnetic field sensor having attached thereto binding molecules which selectively bind the target molecular species;

- magnetizable label particles bearing binding molecules which:

(1) selectively bind the target molecular species or, in the alternative,

(2) selectively bind the sensor bound binding molecules, and

(i) compete for said selective binding of said sensor bound binding molecules with said selective binding of said target molecular species to said sensor bound binding molecules, or

(ii) are displaced from said sensor bound binding molecules by said selective binding of said target molecular species to said sensor bound binding molecules,

whereby the label particles attach to the magnetic field sensor as a result of said selective binding;

- magnetizing means for magnetizing the attached label particles; and

- detection means for monitoring a magnetoresistive or magnetostrictive response of the magnetic field sensor to a magnetic field produced by one or more magnetized label particles attached to said magnetic field sensor, whereby the concentration of the target molecule is determined.

58. An apparatus according to Claim 57, wherein the magnetizable label comprises one or more materials selected from the group consisting of paramagnetic, superparamagnetic, ferromagnetic, and ferrimagnetic materials.

59. An apparatus according to Claim 58, wherein the magnetizable label comprises superparamagnetic, iron oxide-impregnated polymer beads.

60. An apparatus according to Claim 57, wherein the magnetic field sensor comprises a magnetoresistive material.

61. An apparatus according to Claim 60, wherein the magnetoresistive material is anisotropic magnetoresistive; giant magnetoresistive; or colossal magnetoresistive.

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62. An apparatus according to Claim 57, wherein the magnetic field sensor is magnetostrictive.

63. An apparatus according to Claim 57, wherein the magnetic field sensor is a magnetoresistive element made by patterning a magnetoresistive film.

64. An apparatus according to Claim 57, wherein there are a plurality of magnetic field sensors.

65. An apparatus according to Claim 64, wherein each magnetic field sensor detects the presence or absence of a single label particle attached to said magnetic field sensor.

66. An apparatus according to Claim 57, further comprising means to add the target molecules and the magnetizable particles to the sensor.

67. An apparatus according to Claim 57, wherein the magnetizing means is a magnetic field generator and preferably a wire coil, a straight wire, a conductive microfabricated trace, or a permanent magnet.

68. An apparatus according to Claim 57, further comprising means to remove nonspecifically-bound label particles.

69. An apparatus according to Claim 68, wherein the nonspecifically-bound label particles are removed by a means for applying a magnetic force to the particles and preferably an electromagnet, an air-cored coil, or a permanent magnet.

70. An apparatus according to Claim 69, wherein the means to apply the magnetic force is the magnetizing means for magnetizing the label particles.

71. An apparatus according to Claim 57, wherein the binding molecules are antibodies; poly- or oligo-nucleotides, i.e. DNA or RNA; proteins; synthetic polypeptides; or chelators.

72. An apparatus according to Claim 57, wherein the target molecules are selected from the group consisting of polynucleic acids, proteins, metal ions, and low molecular weight organic species such as toxins, illicit drugs, and explosives.

73. An apparatus according to Claim 57, wherein the detection means comprises a Wheatstone bridge for monitoring both a magnetic field sensor having closely-attached binding elements and an identical field sensor without binding elements.

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74. A method for detecting the presence of a target molecular species in a sample suspected of including said target species, comprising the steps of:

a) providing a detector comprising a magnetoresistive or magnetostrictive magnetic field sensor having binding molecules which selectively bind to the target molecules and which are bound to the sensor;

b) bringing the sample and one or more species of magnetizable label particles into contact with the detector at the same or at different times, said label particles having attached binding molecules that;

(1) selectively bind the target species, or, in the alternative;

(2) selectively bind the sensor-bound binding molecules, and

(i) compete for said selective binding of said sensor-bound binding molecules with said selective binding of said target molecular species to said sensor-bound binding molecules, or

(ii) are displaced from said sensor-bound binding molecules by said selective binding of said target molecular species to said sensor-bound binding molecules,

whereby said label particles attach to the sensor as a result of said selective binding, the number of said label particles attached to said sensor being related to the concentration of the target species;

c) removing unbound label particles;

d) magnetizing the remaining bound label particles; and

e) monitoring a magnetoresistive or magnetostrictive response of said magnetic field detector to a magnetic field produced by one or more magnetized label particle attached to said magnetic field sensor, whereby the concentration of the target molecule is determined.

75. A method according to Claim 74, wherein the magnetizable label comprises one or more materials selected from the group consisting of paramagnetic, superparamagnetic, ferromagnetic, and ferrimagnetic materials.

76. A method according to Claim 75, wherein the magnetizable label comprises superparamagnetic iron oxide-impregnated polymer beads.

77. A method according to Claim 74, wherein the magnetic field sensor comprises a magnetoresistive material.

78. A method according to Claim 77, wherein the magnetoresistive material is anisotropic magnetoresistive; giant magnetoresistive; or colossal magnetoresistive.

79. A method according to Claim 74, wherein the magnetic field sensor is magnetostrictive.

80. A method according to Claim 74, wherein the magnetic field sensor is a magnetoresistive element made by patterning a magnetoresistive film.

81. A method according to Claim 74, wherein there are a plurality of magnetic field sensors.

82. A method according to Claim 81, wherein each magnetic field sensor detects the presence or absence of a single label particle attached to said magnetic field sensor.

83. A method according to Claim 74, wherein the bound label particles in step (d) are magnetized by a magnetic field generator and preferably by a wire coil, a straight wire, a conductive microfabricated trace, or a permanent magnet.

84. A method according to Claim 74, wherein the unbound label particles are removed by applying a magnetic force to the particles and preferably by an electromagnet, an air-cored coil, or a permanent magnet.

85. A method according to Claim 84, wherein the magnetic force is applied by the magnet field generator for magnetizing the label particles.

86. A method according to Claim 74, wherein the binding molecules are antibodies; poly- or oligo- nucleotides, i.e. DNA or RNA; proteins; synthetic polypeptides; or chelators.

87. A method according to Claim 74, wherein the target molecules are selected from the group consisting of polynucleic acids, proteins, metal ions, and low molecular weight organic species such as toxins, illicit drugs, and explosives.

88. A method according to Claim 74, wherein the monitoring in step (e) uses a Wheatstone bridge for monitoring both a magnetic field sensor having closely-attached binding elements and an identical field sensor without binding elements.

89. A method according to Claim 74, wherein the contacting in step (b) is done by placing said sample in a solution, applying the solution to the detector, then applying a second solution containing one or more species of magnetizable label particles, wherein said particles have attached label-bound binding molecules with a selective binding response to the target molecules, whereby in the presence of said target molecules said label-bound binding molecules and said sensor-bound binding molecules will sandwich said target molecule, thereby forming a link between said magnetizable label particle and said sensor.

90. An apparatus for sensing a molecule having a magnetic member attached thereto, the magnetic member producing a magnetic field, the apparatus comprising:

- a first magnetoresistive member;
- a first molecular receptor including a first chain of a plurality of nucleotides complementary to a second chain of a plurality of nucleotides of the molecule, the first molecular receptor attached to the first magnetoresistive member so that when the molecule is bound with the first molecular receptor, the magnetic field from the magnetic member influences a magnetization-dependent characteristic of the first magnetoresistive member in accordance with a giant magnetoresistance effect; and
- a readout device coupled to the first magnetoresistive member to produce an electrical signal dependent upon the magnetization-dependent characteristic of the first magnetoresistive member when the molecule is bound with the molecular receptor.

91. The apparatus of Claim 90 wherein the first molecular receptor includes at least one DNA probe, wherein the molecule includes a DNA molecule, and wherein the at least one DNA probe is complementary to the DNA molecule.

92. The apparatus of Claim 90 further comprising a substrate, wherein the readout device includes a transistor integrated with the substrate, and wherein the transistor is coupled to the first magnetoresistive member.

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93. The apparatus of Claim 90 further comprising:

- a second magnetoresistive member; and
- a second molecular receptor attached to the second magnetoresistive member, the second molecular receptor non-specific to the molecule.

94. The apparatus of Claim 93 wherein the second molecular receptor includes a third chain of a plurality of nucleotides non-complementary to the second chain.

95. The apparatus of Claim 93 further comprising a substrate having the first magnetoresistive member and the second magnetoresistive member integrated therewith.

96. A method of sensing a molecule having a magnetic member attached thereto, the method comprising the steps of:

- providing the molecule having the magnetic member attached thereto, the magnetic member producing a magnetic field;
- providing a magnetoresistive member;
- providing a molecular receptor specifically bindable with the molecule, the molecular receptor attached to the magnetoresistive member so that when the molecule is bound with the molecular receptor, the magnetic field from the magnetic member influences a magnetization-dependent characteristic of the magnetoresistive member in accordance with a giant magnetoresistance effect; and
- sensing the magnetization-dependent characteristic of the magnetoresistive member when the molecule is bound with the molecular receptor.

97. The method of Claim 96 wherein the magnetic member has a form of a bead.

98. The method of Claim 96 wherein the molecular receptor includes a chain of a plurality of nucleotides, and wherein the molecule includes a complementary chain of a plurality of nucleotides.

99. The method of Claim 98 wherein the molecular receptor includes at least one DNA probe, wherein the molecule includes a DNA molecule, and wherein the at least one DNA probe is complementary to the DNA molecule.

100. The method of Claim 96 wherein the molecule and the molecular receptor include a complementary antibody-antigen specific binding pair.

101. The method of Claim 96 wherein the step of sensing the magnetization-dependent characteristic of the magnetoresistive member includes sensing a magnetization-dependent conductance of the magnetoresistive member.

102. The method of Claim 101 further comprising the steps of:

providing a readout device coupled to the magnetoresistive member; and

producing an electrical signal indicative of the magnetization-dependent conductance of the magnetoresistive member using the readout device.

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